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ORIGINAL RESEARCH

Effect of Incorporating 1 Avocado Per Day Versus Habitual Diet on Visceral Adiposity: A Randomized Trial

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BACKGROUND: Excess visceral adiposity is associated with increased risk of cardiometabolic disorders. Short-term well-controlled clinical trials suggest that regular avocado consumption favorably affects body weight, visceral adiposity, and satiety.

METHODS AND RESULTS: The HAT Trial (Habitual Diet and Avocado Trial) was a multicenter, randomized, controlled parallel-arm trial designed to test whether consuming 1 large avocado per day for 6 months in a diverse group of free-living individuals (N=1008) with an elevated waist circumference compared with a habitual diet would decrease visceral adiposity as measured by magnetic resonance imaging. Secondary and additional end points related to risk factors associated with cardiometabolic disorders were assessed. The primary outcome, change in visceral adipose tissue volume during the intervention period, was not significantly different between the Avocado Supplemented and Habitual Diet Groups (estimated mean difference (0.017 L [−0.024 L, 0.058 L], *P*=0.405). No significant group differences were observed for the secondary outcomes of hepatic fat fraction, hsCRP (high-sensitivity C-reactive protein), and components of the metabolic syndrome. Of the additional outcome measures, modest but nominally significant reductions in total and low-density lipoprotein cholesterol were observed in the Avocado Supplemented compared with the Habitual Diet Group. Changes in the other additional and post hoc measures (body weight, body mass index, insulin, very low-density lipoprotein concentrations, and total cholesterol:high-density lipoprotein cholesterol ratio) were similar between the 2 groups.

CONCLUSIONS: Addition of 1 avocado per day to the habitual diet for 6 months in free-living individuals with elevated waist circumference did not reduce visceral adipose tissue volume and had minimal effect on risk factors associated with cardiometabolic disorders.

REGISTRATION: URL: https://clinicaltrials.gov; Unique identifier: NCT03528031.

Key Words: avocado ■ habitual diet ■ randomized clinical trial ■ risk factors for cardiometabolic disorders ■ visceral fat

In the United States, ≈60% of adults have visceral adiposity, defined as a waist circumference of ≥40 inches for women and ≥35 inches for men.[1,2] Visceral adiposity is associated with elevated risk of type 2 diabetes, insulin resistance, systemic inflammation, cardiovascular disease, and all-cause mortality.[3–6] To reduce the burden of these chronic disorders, strategies are needed to prevent the development of visceral adiposity.

Independent of total caloric intake, diet quality has been reported to affect visceral adiposity.[7–9] One food of recent interest is avocados. Avocados are a good

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CLINICAL PERSPECTIVE

What Is New?

- In individuals with elevated waist circumference, consuming 1 large avocado per day (Avocado Supplemented Diet) for 6 months compared with habitual diets (Habitual Diet) had no significant effect on visceral adipose tissue volume.
- At the end of the 6-month intervention period, changes in hepatic fat fraction, high-sensitivity C-reactive protein, components of the metabolic syndrome, body weight, body mass index, insulin, very low-density lipoprotein concentrations, and total cholesterol:high-density lipoprotein cholesterol ratio were similar between the Avocado Supplemented and Habitual Diet groups.

What Are the Clinical Implications?

- Consistent with prior observations, a change in dietary patterns rather than a single food or nutrient may be necessary to achieve clinically significant improvements in visceral adiposity and other cardiometabolic risk factors.

Nonstandard Abbreviations and Acronyms

HAT	Habitual Diet and Avocado Trial
HEI	Healthy Eating Index
VAT	visceral adipose tissue

source of fiber and oleic acid, a monounsaturated fatty acid (MUFA). Observational data have linked avocado intake with lower rates of metabolic syndrome.[10,11] A National Health and Nutrition Examination Survey analysis (2001–2012) reported that avocado consumers weighed less (–3.4 kg) and had smaller waist circumferences (–1.2 cm) than nonconsumers.[10] Data from a randomized clinical trial in overweight adults reported that consumption of half an avocado at the lunch meal was associated with higher postprandial satiety and lower desire to eat after 5-hours.[12] However, in another study,[13] inclusion of 1 avocado a day, compared with no avocado, as part of a hypocaloric weight loss diet had no significant effect on weight loss, body mass index, total body fat, or visceral adipose tissue (VAT) despite higher reported levels of satiety.[13] A more recent intervention study also reported that in individuals with a body mass index ≥25 kg/m^2, 1 avocado a day compared with an isocaloric diet with no avocados resulted in no significant difference in change in abdominal adiposity as measured by dual energy x-ray absorptiometry (DEXA).[14] Interestingly, exploratory analyses suggested there might be a decrease in abdominal adiposity and ratio of VAT to subcutaneous abdominal adipose tissue in women but not men.

The aim of this study was to determine whether providing 1 avocado a day for 6 months compared with the habitual diet would alter VAT volume, hepatic fat fraction, systemic inflammation (hsCRP [high sensitivity C reactive protein]), and components of the metabolic syndrome in individuals with an elevated waist circumference. Our hypothesis was that addition of an avocado daily to participants' habitual diet would improve these outcomes.

METHODS

The data supporting this article are available from the Hass Avocado Board by request.

Study Design and Oversight

The HAT Trial (Habitual Diet and Avocado Trial) was a randomized, controlled, parallel-arm, unblinded study conducted at 4 clinical centers in the United States. A trial coordinating center provided data management and statistical support. In addition, there was a central laboratory, magnetic resonance imaging (MRI) reading center, and 2 diet assessment centers (Data S1). A detailed description of the study design has been published.[15] The trial is registered at https://clinicaltrials.gov (NCT03528031).

The Hass Avocado Board sponsored the trial and provided avocados but did not have access to the data files at any time, blinded or unblinded. A steering committee consisting of principal investigators from the 4 clinical centers and the coordinating center provided oversight for the trial. There was no external monitoring board or analysis of interim results. The study was given initial approval by institutional review boards at each center and then administered by the coordinating center institutional review board.

Study Population

Inclusion criteria were ≥25 years, waist circumference ≥35 inches for women and ≥40 inches for men, and regular consumption of ≤2 avocados per month. Exclusion criteria were aversion to avocados, known avocado sensitivity, and unwillingness to undergo MRI scans. Additional criteria are included in Table S1. All participants provided written informed consent.

Randomization and Intervention

Eligible participants were randomly assigned to either a group who were given 1 avocado per day to consume (Avocado Supplemented Diet Group) or a group who continued their usual diet (Habitual Diet

Group). Group assignment was determined using permuted block randomization with varying block sizes of 4 and 8 and stratification by clinical center. Allocation was concealed by using an interactive web response system for participant randomization. Neither participants nor clinical center staff were blinded to intervention assignment. The MRI reading center and central laboratory staff were blinded to intervention assignment.

Participants in the Avocado Supplemented Diet Group were instructed to follow their habitual diet and lifestyle, regularly provided with fresh Hass avocados to allow consumption of 1 per day for the 6-month intervention period. Staff provided participants with written instructions describing how to ripen, cut, remove the pit of, and peel avocados, as well as serving ideas and recipes containing avocados. No additional dietary counseling or guidance was provided.

Participants in the Avocado Supplemented Diet Group picked up avocados from their study site every 2 weeks, during which interaction with study personnel was minimized. Participants in the Habitual Diet Group were instructed to follow their habitual diet and lifestyle and limit their avocado intake to ≤2 avocados/month.

Study Measurements and Outcomes

Apart from the biweekly avocado pickup of the Avocado Supplemented Diet Group, all participants were seen every 4 weeks through week 20, with a final visit at week 26. An extension of the 6-month study period was needed toward the end of the trial because of the COVID-19 pandemic. Avocados were delivered to participants still in the trial during the temporary research pause mandated at the clinical sites, which halted the collection of end point measurements until subsequent approval was granted to collect the final data.

Demographic data were collected at baseline. Weight, waist circumference, health-related quality of life, and blood samples were collected at baseline and 12 and 26 weeks. Twenty-four hour dietary intake data were collected using Nutrition Data System for Research (software versions 2017 and 2018) at baseline and 8, 16, and 26 weeks. These data were used to assess compliance, estimate energy and nutrient intake, and calculate the Healthy Eating Index (HEI) 2015.[16] The RAND 36-Item Health survey was used to assess health-related quality of life.[17]

Safety data were collated by the coordinating center. Food sensitivity to avocado consumption, although uncommon, has been reported and staff were trained to refer participants to their primary care physician if they suspected an adverse reaction. Unexpected events involving a hospitalization were reported to the central institutional review board by the coordinating center.

The primary hypothesis was that providing 1 avocado per day for 6 months to participants in the Avocado Supplemented Diet Group would result in a reduction in visceral adiposity measured by MRI compared with the Habitual Diet Group. Secondary measures included hepatic lipid content, plasma hsCRP concentrations and components of the metabolic syndrome (plasma glucose, triglyceride and high-density lipoprotein cholesterol [HDL-C] concentrations, blood pressure, and waist circumference). Additional measures included plasma insulin, total cholesterol and low-density lipoprotein cholesterol (LDL-C) concentrations, fiber, HEI, and health-related quality of life.

MRI Collection and Analysis

Participants underwent 2 abdominal MRI scans, 1 before randomization and 1 at the end of the nominal 6-month intervention. MRI data were collected on 3T Skyra or Prisma scanners (Siemens Healthineers, Erlangen, Germany) using 7 different scanners at 5 imaging centers near the clinical sites. Two ex vivo preserved human livers, and a fat/water phantom were scanned at all sites to verify that consistent data were collected across all sites and over time. The ex vivo livers were formalin fixed, 1 chosen from an individual with no history of liver pathology and 1 with a history of nonalcoholic fatty liver disease. The fat/water phantom was an ≈4 L container that contained about 3.2 L of 5% agarose gel with 0.03% sodium azide, and 0.8 L of lard. VAT volume was assessed using a 2-echo DIXON 3-dimensional axial vibe sequence with field of view=400 mm, repetition time=5 ms, echo time=1.23, 2.46 ms, fractional anisotropy=9°, resolution=2.1×2.3×3.5 mm^3, and acquisition time=17 seconds in a single breath hold. Slice coverage was enough to cover 4 cm above the dome of the liver to 7 cm below the top of the iliac crest. Hepatic fat fraction was assessed with point resolved spectroscopy sequence with repetition time=2000 ms, echo time=20 ms, Nx=8, and acquisition time=16 seconds in a single breath hold. This approach has a high level of precision[18] and provides detailed 3-dimensional images of the abdomen that allow for quantification of even small (a few millimeters) collections of fat (Figure S1).

The MRI data collected at each site were anonymized and sent to the MRI reading center for centralized analysis. All analyses were performed blinded to treatment group. Dixon fat images for VAT volume were manually segmented to exclude subcutaneous fat using SliceOmatic and a watershed algorithm. Images were then thresholded using an implementation of the Otsu algorithm from ImageJ. Threshold results were manually reviewed and any nonvisceral fat (such as from the vertebral bodies) was manually removed. MR spectroscopy was processed with LCModel version

6.3 using lipid quantification settings, and T1 and T2 correction were applied.[19]

Biochemical Measures

Details regarding measurement of blood pressure, anthropometric measures, dietary assessment, and quality of life survey have been reported previously.[15] Briefly, blood sample (serum, plasma, red blood cells, and buffy coat) collection was standardized at all sites as per instructions in the *Blood Processing Manual of Operation Procedures*. Plasma total cholesterol, HDL-C, triglyceride, and glucose concentrations were measured using an automated clinical chemistry analyzer (AU480, Beckman Coulter Inc., CA) with intra-assay coefficients of variability of 2.0% to 3.0% and interassay coefficients of variability of 2.8% to 5%.[20–22] LDL-cholesterol concentrations were calculated using the Friedewald formula,[23] except when triglyceride concentrations were over 400 mg/dL, in which case a direct LDL-C 2 reagent colorimetric enzymatic assay was used (AU480, Beckman Coulter, Inc., CA) with intra- and interassay coefficients of variability of 2.4% and 3.6% respectively. very LDL-C concentrations were calculated as triglycerides/2.2. Serum insulin and hsCRP concentrations were measured by solid-phase, 2-site chemiluminescent immunometric assays (IMMULITE 2000, Siemens Healthcare Diagnostics, Los Angeles, CA).[24] The intra- and interassay coefficients of variability were 3.0% and 5.0%, respectively for hsCRP and 3.5% and 5.0%, respectively, for insulin. Details regarding measurement of blood pressure, anthropometric measures, dietary assessment, and quality of life survey have been reported previously.[15]

Statistical Analysis

The trial was designed to randomize 1000 participants over a 2-year period and assumed a 10% lost to follow-up rate. It was estimated that this sample size would provide 85% power to detect a 6-month between-group change in VAT volume of 0.5 L favoring the Avocado Supplemented Diet group. The prespecified primary analysis was an intent-to-treat comparison of the 2 randomized groups on the estimated 6-month change in VAT volume, restricted to participants with complete data. The effect on change in VAT volume from baseline to follow-up was estimated using a linear regression adjusted for randomized group and site, and primary hypothesis testing was 2 sided with α=0.05. Supporting analyses were done using all available VAT measurements at both baseline and follow-up in a mixed effects model adjusting for randomized group and site to estimate the 6-month effect on VAT. Prespecified subgroups of interest were defined using sex, ethnicity or race (non-Hispanic White versus other [Native Hawaiian, Pacific Islander, or Other]), baseline VAT (median split), baseline HEI (median split), and baseline kilocalorie intake (median split). Subgroup hypotheses were tested by adding a categorical subgroup indicator to the linear regression model and an interaction term for intervention by subgroup. The significance of the interaction term adjusted for multiple comparisons was used to test for subgroup effects.

Effects on secondary and other measures were estimated with models on change from baseline similar to the primary analysis but using mixed effects when multiple postrandomization assessments were done. Effects averaged over the follow-up period are reported when there is no significant time by intervention interaction. For these effects, reported *P* values are nominal; no adjustment for multiple comparisons was made. For the 24-hour diet recall data, mixed effects models adjusted for randomized group and clinic for all available measurements were used to estimate visit-specific means and the mean difference from baseline over follow-up. Descriptive statistics are reported as means and SD except for highly skewed distributions, where median, first, and third quartiles are reported. Counts and categorical data are summarized as N and %.

RESULTS

Study Participants

From June 27, 2018 to March 4, 2020, 1008 participants were randomly assigned to either the Avocado Supplemented Diet Group or Habitual Diet Group (Figure 1). A total of 85 participants did not complete the follow-up MRI, 50 in the Avocado Supplemented Diet Group and 35 in the Habitual Diet Group. At the time of randomization, participants mean age was 50 (14) (mean [SD]) years (Table 1) and 72% were women. The racial and ethnic distribution of the cohort was 68.8% White, 20.6% Hispanic, 14.8% Black, 5.8% Asian, and 10% either did not answer, were American Indian, other or multiple races or ethnicities. The mean waist circumference of women was 106 (12) cm and men 118 (12) cm. The mean VAT was 3.2 (1.4) liters and hepatic fat fraction 9.9 (11) %. Follow-up measures were completed in October 2020. Of the 935 (93%) participants with final MRI scans, 12 were not readable, leaving 923 (92% of the randomized participants) with complete data.

Compliance With the Intervention

Participants from both intervention groups reported infrequent intake of avocado at baseline (Table 2). No significant in-trial differences in avocado consumption were observed in the Habitual Diet Group, whereas the Avocado Supplemented Diet Group increased intake and maintained a high level of consumption. Based on self-reported 24-hour diet recalls during the follow-up period, among the Avocado Supplemented Diet Group

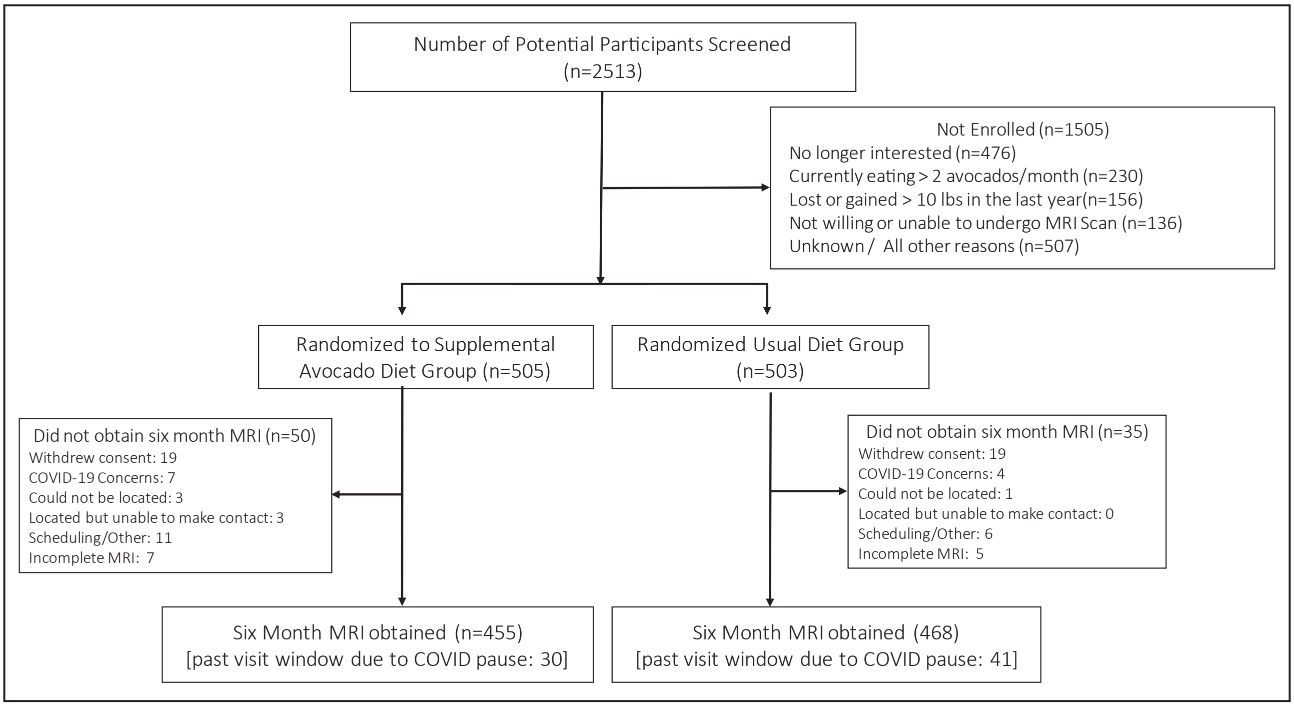

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) diagram.
MRI indicates magnetic resonance imaging.

participants, 76% to 78% consumed at least 1 whole avocado and 12% to 17% consumed some avocado (total 88%–95%) each day. In contrast, 92% to 94% of the Habitual Diet Group participants reported consuming no avocado and the remainder only some avocado.

Diet Composition Intake

The daily energy intake remained stable for the Habitual Diet Group and significantly increased at weeks 8, 16, and 26 for the Avocado Supplemented Diet Group. During the intervention, dietary fiber, fat (total fat and MUFA, both g per day and % energy), and HEI were significantly higher in the Avocado Supplemented Diet Group than the Habitual Diet Group (Table S2). Dietary carbohydrate and protein intake were significantly lower in the Avocado Supplemented Diet Group than the Habitual Diet Group.

Change in Primary, Secondary, and Additional Measures

The primary outcome, change in VAT volume from baseline to 6 months, was similar between diet groups; 0.074 L in the Avocado Supplemented Diet Group and 0.057 L in the Habitual Diet Group (*P*=0.405; Table 3, Table S3, Figure S2). The estimated mean difference was 0.017 L (−0.024 L, 0.058 L, mean and CIs). The effect of the intervention was consistent across prespecified participant subgroups (Figure 2, Table S4). Inclusion of all available MRI data, including participants who did not have final MRI measures, did not significantly affect this result (Data S1).

Providing 1 avocado per day for 6 months resulted in no significant differences in changes between the 2 groups for the secondary outcomes of hepatic fat fraction, hsCRP, or components of the metabolic syndrome (waist circumference, systolic and diastolic blood pressure, or triglyceride, glucose, and HDL-C concentrations) (Table 3). Of the additional outcomes, only total cholesterol and LDL-C were nominally significant, modestly lower in the Avocado Supplemented compared than Habitual Diet Group (2.9 [*P*=0.026] and 2.5 mg/dL [*P*=0.038], respectively). The other additional and post hoc outcomes, body mass index, insulin, and very LDL-C concentrations, and total cholesterol:HDL-C ratio were similar in the Avocado Supplemented and Habitual Diet Groups. There was a significant increase in fiber and the HEI in the Avocado Supplemented Diet Group compared with the Habitual Diet Group and no significant effect on body weight, which remained stable during the intervention period in both groups (Tables 3 and 4, Table S2).

Adverse Events

There were 21 adverse events reported during the trial, 16 occurred in the Avocado Supplemented Diet Group and 5 occurred in Habitual Diet Group (Table 5). Twelve events were unrelated to trial participation. Nine events were identified as possibly or definitely related to the intervention, all in the Avocado Supplemented Diet Group, and

Table 1. Baseline Characteristics of Study Participants

Variables*	Overall (N=1008)	Study arms: Avocado Supplemented Diet Group (n=505)	Study arms: Habitual Diet Group (n=503)
Age, y	50.3±14.0	50.1±14.3	50.4±13.8
Women, n (%)	730 (72.4)	356 (70.5)	374 (74.4)
Hispanic or Latino, n (%)	207 (20.6)	106 (21.0)	101 (20.2)
Race, n (%)			
Did not answer	3 (0.3)	1 (0.2)	2 (0.4)
Black	149 (14.8)	68 (13.5)	81 (16.1)
American Indian	4 (0.4)	2 (0.4)	2 (0.4)
Asian	58 (5.8)	26 (5.1)	32 (6.4)
White	694 (68.8)	361 (71.5)	333 (66.2)
Other†	72 (7.1)	33 (6.5)	39 (7.8)
Multiple races reported	28 (2.8)	14 (2.8)	14 (2.8)
Anthropometric measures			
Weight, kg	93.2±19.0	93.2±19.0	93.1±18.9
Body mass index, kg/m^2	33.0±5.5	32.9±5.3	33.2±5.6
Waist circumference, cm	109±13	109±13	109±13
Women	106±12	106±12	107±12
Men	118±12	118±12	118±12
Biochemical measures, mg/dL			
Total cholesterol	188±40	185±40	190±39
LDL-cholesterol	112±34	110±34	114±34
HDL-cholesterol			
Women	55±13	55±13	56±13
Men	45±10	44±9	45±10
Very LDL-cholesterol	21 (15, 29)	21 (16, 29)	21 (15, 29)
Triglyceride	104 (76, 145)	106 (79, 145)	104 (73, 145)
Total cholesterol:HDL-cholesterol	3.7±1.0	3.8±1.0	3.7±1.0
Glucose, mg/dL	107±29	107±29	107±30.0
Blood pressure, mm Hg			
Diastolic	77±10	77±10	76±11
Systolic	123±16	123±16	123±16
Magnetic resonance imaging measures			
Visceral adipose tissue, L	3.2±1.4	3.2±1.4	3.2±1.4
Hepatic fat fraction, %	9.9±10.6	9.5±9.9	10.2±11.2

HDL indicates high-density lipoprotein; and LDL, low-density lipoprotein.
*Continuous data are presented as mean±SD, or median (first quartile, third quartile). Categorical variables are presented as number and percent.
†Other indicates Native Hawaiian, Pacific Islander, or Other.

included experiencing skin rash or breathing difficulties (n=3) and gastrointestinal upset (gas, bloating, diarrhea) (n=6). Two were classified as serious, 1 for noncardiac chest pain and 1 for *E coli* infection. Both resolved and did not recur. No deaths occurred during the trial.

DISCUSSION

In a large multicenter study of 1008 free-living participants with elevated waist circumference, addition of 1 avocado a day for 6 months to habitual diets had no effect on VAT volume, the primary study end point, despite a positive effect on diet quality. Subgroup analyses showed a consistently null effect across sex, race or ethnicity, baseline VAT, baseline energy intake, and baseline HEI and health-related quality of life. Changes in most secondary and additional outcome measures (cardiometabolic risk factors), except for modest decreases in total cholesterol and LDL-C concentrations, were not statistically significant.

The hypothesis that avocado intake would reduce VAT was based on prior clinical trials reporting that diets high in MUFA lowered the upper body fat (android and

Table 2. Avocado Intake by Intervention Group, Percentage*

Avocado intake	Avocado Supplemented Group (n=504)				Habitual Diet Group (n=503)			
	Baseline	Intervention			Baseline	Intervention		
		8 wk	16 wk	26 wk		8 wk	16 wk	26 wk
	Percent participants*							
None	90.9	4.9	8.1	11.9	91.7	94.2	92.8	91.5
Some†	8.1	16.7	15.7	12.1	8.1	5.6	7.2	8.3
One+/d	1.0	78.4	76.2	76.1	0.2	0.2	0.0	0.2

*Percentage data from 24-hour diet recalls collected for specified week by treatment arm.
†Some defined as avocado consumption reported in the recall was <90% of the study-provided amount of 168 g (151 g): total avocado <151 g; avocado reported but no amount given; avocado on toast, bread, salad, sandwich, etc but no amount given and no note for amount, and guacamole reported in the recall was less than the Nutrition Data System for Research equivalent to 168 g of avocado (1.5 cups); total guacamole <1.5 cups; and guacamole reported but no amount given.

abdominal) to lower body fat (gynoid) ratio, both with and without weight loss.[25–28] There were differences between the interventions among these studies. Those reporting this finding involved dietary interventions that achieved levels of MUFA >22% of total caloric intake, used a different source of MUFA, and/or replaced the MUFA with saturated fat.[26–28] Notably, relative to prior studies, the present study had a larger sample size, which increased the statistical power to detect true effects if they occurred, had a longer intervention period, and employed a more realistic dietary modification, a single avocado a day with no additional dietary advice, mimicking real world conditions.

A recent 12-week intervention study of individuals with a body mass index ≥25 kg/m^2, who consumed 1 avocado a day compared with an isocaloric diet with no avocados, also did not observe significant differences in change in abdominal adiposity as measured by DEXA.[14] In that study, exploratory analyses indicated there was a significant decrease in abdominal adiposity and in VAT to subcutaneous abdominal adipose tissue ratio in women but not men. A direct comparison

Table 3. Model-Based Estimates of Change in Prespecified Primary, Secondary, and Additional Outcome Measures by Intervention Group

Outcomes	Supplemented Avocado Diet Group	Habitual Diet Group	Effect	95% CI	*P* value
Primary*					
Visceral adipose tissue, L	0.074	0.057	0.017	−0.024 to 0.058	0.405
Secondary*					
Hepatic fat fraction, %	0.58	0.21	0.37	−0.31 to 1.06	0.285
High-sensitivity C-reactive protein, mg/L	0.788	0.435	0.352	−0.845 to 1.550	0.564
Components of the metabolic syndrome					
Waist circumference, cm	0.007	−0.108	0.116	−0.320 to 0.551	0.603
Systolic BP, mm Hg	−1.286	−0.034	−1.251	−2.566 to 0.064	0.062
Diastolic BP, mm Hg	−1.012	−0.324	−0.688	−1.601 to 0.225	0.139
Triglyceride, mg/dL	2.959	4.069	−1.110	−7.624 to 5.403	0.738
Glucose, mg/dL	0.629	1.577	−0.948	−2.962 to 1.065	0.356
HDL-cholesterol, mg/dL	−0.279	−0.183	−0.096	−0.885 to 0.692	0.811
Additional* and post hoc outcomes					
Body weight, kg	0.382	0.378	0.004	−0.310 to 0.318	0.978
Body mass index, kg/m^2	0.142	0.134	0.009	−0.103 to 0.120	0.880
Insulin, µIU/mL*	0.120	0.615	−0.495	−2.089 to 1.098	0.542
Total cholesterol, mg/dL*	−4.908	−1.968	−2.940	−5.535 to −0.346	0.026†
LDL-cholesterol, mg/dL*	−4.947	−2.482	−2.465	−4.796 to −0.134	0.038†
Very LDL-cholesterol, mg/dL	0.592	0.814	−0.222	−1.525 to 1.081	0.738
Total cholesterol: HDL-cholesterol	−0.083	−0.028	−0.055	−0.119 to 0.009	0.095
Health-related quality of life (0–100)*	0.164	−0.320	−0.481	−1.615 to 0.653	0.405

BP indicates blood pressure; HDL, high-density lipoprotein; and LDL, low-density lipoprotein.
*Pre-specified.

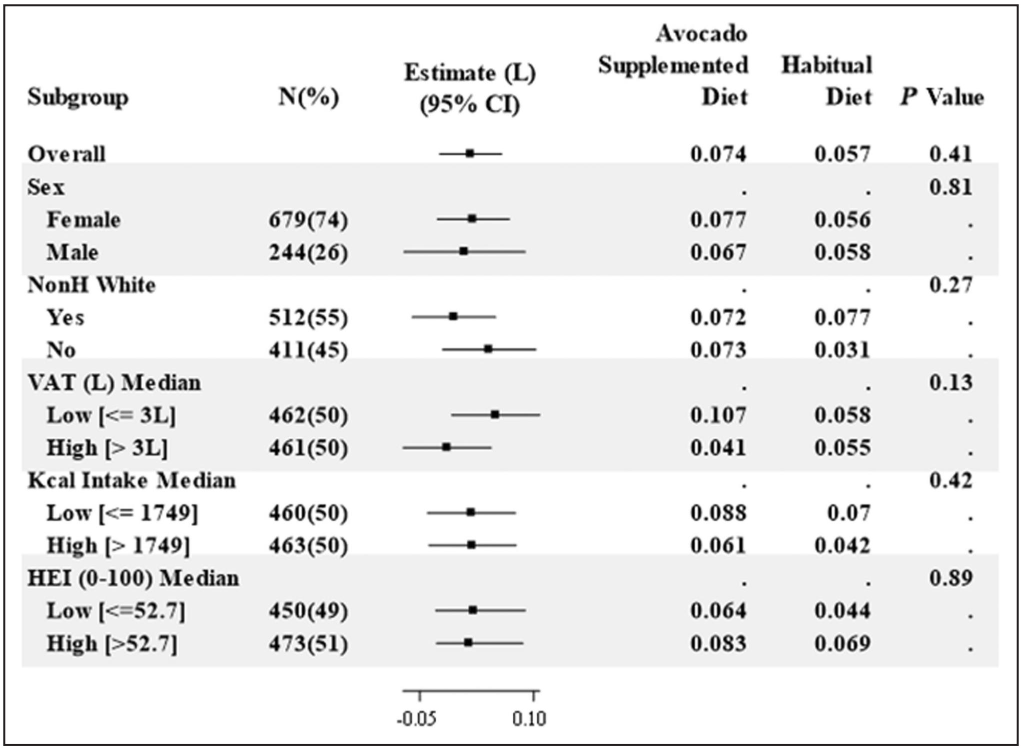

Figure 2. Visceral adipose tissue by subgroup.

For each subgroup, the estimated difference of the 6-month effects on VAT between the Avocado Supplemented Diet group and the Habitual Diet group is shown as a solid square with a horizontal line showing its 95% CI. At the right, the estimated 6-month effect on VAT from the mixed effects model is shown for each group along with a *P* value for the interaction terms, except for Overall, which is the *P* value for the difference. HEI indicates Healthy Eating Index (range from 0 to 100); Kcal, kilocalories; NonH White, Non-Hispanic White; and VAT, visceral adipose tissue volume (in liters).

between the 2 studies cannot be made because the data for our study are expressed as the total intake whereas the data provided in the earlier publication are only for the single meal that contained an avocado. In addition, DEXA was used to assess adiposity in the prior study, whereas multislice 3-dimensional MRI was used to measure VAT in the current study. Although cheaper and faster, DEXA measures are limited to providing a single 2-dimensional projection image. Although comparison studies have shown DEXA to perform similarly to single-slice MRI in cross-sectional studies,[29] it does not perform well in longitudinal studies and is likely to underestimate small longitudinal changes.[30,31] Despite providing no guidance with regard to offsetting the energy content of the avocados, there was no significant effect of the avocados on body weight, suggesting participant nonintentional compensation. The compensation resulted in a shift in macronutrient content of the diet during the 6-month intervention period. The participants in the Avocado Supplemented Group increased their fat and lowered their carbohydrate and protein intake.

Nominally significant greater decreases in total cholesterol and LDL-C concentrations were observed in the Avocado Supplemented compared with Habitual Diet Group. The between-group differences in total cholesterol and LDL-C align with the observed dietary fiber differences between groups. A single avocado has ≈3.3 g of soluble fiber.[32] Other factors may have also contributed to the differences in total cholesterol and LDL-C concentrations, such as changes in the gut microbiota[33] and the phytosterol content of the avocados.[34] The findings of the current study are in contrast with those of a systematic review that included data up to February 2015,[35] which concluded avocados decreased total cholesterol and LDL-C and resulted in no significant change in HDL-C, and one that included data up to September 2017,[36] which concluded avocados did not decrease total and LDL cholesterol but increased HDL-cholesterol concentrations. Differences in inclusion and exclusion criteria, in addition to the period searched, may explain the differences. An observational study published in 2022 focusing on 2 large US cohorts concluded that dietary patterns containing avocados were associated with lower cardiovascular disease risk and coronary heart disease when replacing foods such as margarine, butter, egg, yogurt, cheese, and processed meats.[37]

Table 4. Descriptive Statistics of Secondary and Additional Measures

Variable	Avocado Supplemented Diet Group (n=505)			Habitual Diet Group (n=503)		
	Baseline	Intervention		Baseline	Intervention	
		3 mo	6 mo		3 mo	6 mo
Anthropometric						
Body weight, kg	93.2±19.0	93.8±19.3	93.4±19.4	93.1±18.9	93.6±19.1	93.4±19.1
Body mass index, kg/m^2	32.9±5.3	33.1±5.5	33.0±5.5	33.2±5.6	33.3±5.7	33.2±5.6
Waist circumference, cm*						
Women	106.0±11.9	106.1±12.2	106.3±12.6	106.6±12.2	106.6±12.6	106.3±3.0
Men	117.6±11.5	117.6±11.8	116.8±12.0	117.6±12.2	117.6±12.6	117.2±12.7
Cardiometabolic risk factors						
Systolic BP, mm Hg*	123±16	121±15	122±16	123±16	122±15	123±16
Diastolic BP, mm Hg*	77±10	75±10	76±15	76±11	76±10	76±10
High-sensitivity C-reactive protein, mg/L*	3.7 (1.5–7.8)	3.7 (1.5–7.6)	3.6 (1.6–7.6)	3.7 (1.6–7.3)	3.7 (1.4–7.7)	3.8 (1.6–7.9)
Total cholesterol, mg/dL†	185±40	181±40	180±38	190±39	189±40	189±38
LDL-cholesterol, mg/dL†	110±34	106±33	104±33	114±34	112±34	111±33
HDL-cholesterol, mg/dL*						
Women	55±13	55±13	54±13	56±13	56±12	56±13
Men	44±9	45±10	44±9	45±10	46±11	46±11
Very LDL-cholesterol, mg/dL	21 (16–29)	20 (15–29)	21 (15–30)	21 (15–29)	21 (15–30)	21 (16–29)
Triglyceride, mg/dL*	106 (79–145)	102 (73–144)	103 (75–148)	104 (73–145)	105 (76–149)	104 (80–146)
Total cholesterol:HDL-cholesterol	3.8±1.0	3.7±1.1	3.7±1.0	3.7±1.0	3.7±1.0	3.7±1.0
Glucose, mg/dL*	100 (93–109)	100 (93–108)	101 (94–111)	101 (93–110)	100 (93–109)	101 (94–110)
Insulin, μIU/mL†	14 (9–20)	14 (9–20)	13 (9–21)	13 (8–21)	13 (9–22)	13 (8–22)

Data are presented as mean±SD, or median (interquartile range). BP indicates blood pressure; HDL, high-density lipoprotein; and LDL, low-density lipoprotein.
*Secondary outcome.
†Additional prespecified outcome.

The estimated between-group differences in mean energy intake were significantly higher in the Avocado Supplemented than Habitual Diet Group (117 kilocalories); however, there was no significant difference in change in mean body weight between groups. Self-reports indicated >90% compliance with the intervention. Energy intake was estimated using a subjective measure,[38] the mean of 4 24-hour dietary recalls collected during the 6-month intervention period, whereas body weight was assessed objectively, using a calibrated scale. One large avocado provided in this study contained 280 kilocalories suggesting that avocados at least partially replaced a component of habitual intake. Although the specific food groups replaced by the avocados were not determined, the macronutrient profile data suggest avocados replaced foods relatively high in carbohydrate. Our results are consistent with a systematic review published this year that concluded avocado consumption did not promote weight gain.[39]

Table 5. Safety: Adverse Events, by Arm

Event	Avocado Supplemented Diet*	Habitual Diet
Breathing difficulties, skin rash	3	0
Gastrointestinal	6	0
Other	7	5
Total	16	5

*Two adverse events that occurred in the Avocado Supplemented Diet arm were deemed “possibly” linked to the intervention. One was for noncardiac chest pain and the other for *E coli* infection. Both resolved without further medical intervention and did not recur during the trial.

The HAT study was a large multicenter, investigator-blinded, randomized clinical trial. The retention rate was high (92%), despite the extraordinary challenges associated with the COVID-19 pandemic (Table S5). Changes in the dietary intake of the Avocado Supplemented Diet Group were consistent with what would be predicted based on the macronutrient composition of the fruit. The primary outcome, VAT, was measured prospectively with a high level of precision using a multislice 3-dimensional MRI technique. This trial was not without limitations. Medication usage was not collected. Given the intervention period and frequency of physician visits it is unlikely there were major changes in medication usage in the vast majority of participants. As with all food-based diet trials, participants could not be blinded to the dietary intervention. The 6-month intervention period may have been insufficient to detect a change in VAT. However, a longer intervention period might have compromised compliance. Although an uninterrupted supply of avocados was provided until arrangements for final study measures could be made, the lives and diets of those last enrolled in the trial may have been affected by the COVID-19 pandemic. Were there a change, the concurrent control design likely balanced a potential temporal bias between the 2 groups. The commitment of subjects and research teams at all sites made it possible to successfully complete the study and maintain a high level of dietary compliance.

CONCLUSIONS

In conclusion, in this randomized controlled multicenter parallel trial, the addition of 1 avocado per day to the habitual diet for 6 months in individuals with visceral adiposity did not reduce VAT and had minimal effect on risk factors associated with cardiometabolic disorders.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Data S1
Tables S1–S5
Figures S1–S2

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SUPPLEMENTAL MATERIAL

Data S1.

Supplemental Methods

Supporting analyses of VAT

The primary analysis for HAT included all participants with complete scans at baseline and follow-up. Two supporting analyses were also performed. For the first supporting analysis, all participants with an MRI scan at both baseline and follow-up were included, whether or not the scans were complete. Complete scans included 51 'slices' (see Figure S1) but in some cases motion or other artifacts allowed only a smaller number of scans to be included. The scans were then analyzed with the same model used for the primary analysis. The second supporting analysis included all scans, whether or not they were complete and whether or not they were part of a baseline-follow-up pair. For this model, scans were considered repeated measures within participants and a mixed model with both fixed and random effects was fit. Using model results, least squares estimates of linear contrasts of model parameters were computed for the mean changes in the Supplemented Avocado and Diet and Habitual Diet Groups and the difference of the changes.

All three models produced qualitatively similar results; that is, a small non-significantly larger increase in VAT in the Supplemented Avocado Diet Group. All are consistent with the conclusion that there was no improvement in VAT in the Supplemented Avocado Diet Group Compared to the Habitual Diet Group.

Changes in VAT

Primary and supporting models	**n**	**Supplemented Avocado Diet Group**	**Habitual Diet Group**	**Estimate**	**95% CI**	**p-value**
1. Primary analysis						
All participants with complete follow-up MRI scans	923	0.074	0.057	0.017	-0.024, 0.058	0.405
2. All available pairs						
All participants with follow-up scans, including incomplete scans	935	0.072	0.057	0.015	-0.026, 0.055	0.39
3. All available scans						
All baseline and follow-up scans, complete and incomplete	1008	0.077	0.063	0.014	-0.026, 0.054	0.54

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Table S1. Inclusion and exclusion criteria.

Inclusion Criteria

- Increased waist circumference defined as ≥35 inches for women, ≥40 inches for men (NCEP ATP III 2005)
- At least 25 years old at screening
- Not currently eating more than 2 avocados per month (habitual intake in U.S.)

Exclusion Criteria

- Does not eat avocados
- Sensitive / allergic to avocados
- Allergies to latex or oral allergy syndrome
- Not willing or unable to undergo MRI scans
- Unstable medical condition such as on dialysis for renal disease, cardiac, gastrointestinal, or hepatic disease, cancer (non-melanoma skin cancer >5 years ago acceptable, any cancer site >10yrs without recurrence).
- Pregnant, lactating, intention of pregnancy
- Lost or gained 10 lbs of body weight in last year
- Following restricted or weight loss dietary patterns
- Unstable anti-anxiety / anti-depressive / anti-psychotic medication use defined as dose change within last 6 months
- Oral steroid use within the last 6 months longer than 7 days
- Elevated alcohol intake (7+ drinks/week women; 14+ drinks/week men)
- Participation in another clinical intervention trial within 30 days of baseline
- PI judgment

From: The design and rationale of a multi-center randomized clinical trial comparing one avocado per day to usual diet: The Habitual Diet and Avocado Trial (HAT) [15].

Table S2. **Diet Composition at baseline and during the intervention derived from 24 hour recall at each visit***

Variables	**Avocado Supplemented Diet Group**				**Habitual Diet Group**				**Estimated Mean difference ** **	**p-value**
	Baseline	Intervention			Baseline	Intervention				
		8 wk	16 wk	26 wk		8 wk	16 wk	26 wk		
N	504	490	479	472	503	486	487	480		
Energy, kcal	1889	2046	2053	2029	1839	1874	1873	1880	117	**0.009**
Protein, g	78	77	79	77	82	82	82	79	0.5	0.846
Animal protein, g	51	49	51	49	56	56	56	53	-0.1	0.979
Vegetable protein, g	27	29	28	28	26	26	26	26	0.6	0.523
Protein, %E	17	15	16	16	18	18	18	18	-1.4	**0.001**
Carbohydrates, g	213	212	211	211	202	205	207	205	-4.6	0.406
Carbohydrates, %E	44	40	39	40	43	43	42	43	-4.1	**<0.001**
Fiber, g/d	20	29	29	28	20	19	19	19	9.4	**<0.001**
Fiber, g/1000 kcal	11	15	15	15	11	11	11	11	4	**<0.001**
Fat, g	81	101	100	99	80	81	80	82	18	**<0.001**
Fat, %E	37	43	43	43	38	38	37	38	6.0	**<0.001**
SFA, g	27	29	29	28	26	27	26	27	1.3	0.207
SFA, %E	12	12	12	12	12	12	12	13	0.0	0.945
MUFA, g	29	42	42	42	28	29	28	30	13.0	**<0.001**
MUFA, %E	13	18	18	18	13	13	13	13	5.2	**<0.001**
PUFA, g	19	21	20	20	18	18	18	18	1.4	0.067
PUFA, %E	9	9	8	9	9	8	8	8	0.0	0.988
Omega-3 FA, g	2.0	2.1	2.0	2.1	2.1	2.0	2.0	2.1	0.12	0.286
Omega-6 FA, g	17	18	18	18	16	16	16	16	1.2	0.074
Cholesterol, mg/d	285	285	309	303	313	314	321	321	7.9	0.582
Cholesterol, g/1000 kcal	154	143	153	152	177	174	182	177	-5.3	0.473
Alcohol, %E	2	1.7	2.1	2	1.6	1.6	2	2.3	-0.4	0.128
HEI	53	62	62	62	54	54	54	55	8.4	**<0.001**

* Recalls were collected via phone call within +/- 2-weeks of the intervention visit timepoints

** Estimated mean change from baseline averaged over follow-up. Visit specific values are estimates from a mixed effects model. See Methods.

SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; FA, fatty acid; HEI, healthy eating index.

Table S3. Descriptive Statistics of MRI Measures (mean +/- SD)

Variable	Supplemented Avocado Diet Group (n=505)		Habitual Diet Group (n=503)	
	Baseline	End of Study visit	Baseline	End of Study visit
VAT[1]	3.2 ± 1.4	3.3 ± 1.3	3.2 ± 1.4	3.3 ± 1.4
HFF[2]	9.5 ± 9.9	10.2 ± 10.6	10.2 ± 11.2	10.5 ± 11.0

VAT = visceral adipose tissue volume (in liters); HFF = hepatic fat fraction.

Table S4. **Visceral adipose tissue (VAT) measures by subgroup.**

Subgroups	n	Supplemented Avocado Diet Group	Habitual Diet Group	Estimate	95% CI	p-value
VAT (L) – all participants	923	0.074	0.057	0.017	-0.024, 0.058	0.405
Sex						0.808
Women	679	0.077	0.056	0.020	-0.027, 0.068	
Men	244	0.067	0.058	0.009	-0.071, 0.089	
Non-Hispanic White						0.273
Yes	512	0.072	0.077	-0.005	-0.060, 0.050	
No	411	0.073	0.031	0.041	-0.020, 0.103	
VAT (L)						0.126
Low [<= 3L]	462	0.107	0.058	0.050	-0.008, 0.108	
High [> 3L]	461	0.041	0.055	-0.014	-0.072, 0.044	
Kcal intake						0.425
Low [<= 1749]	460	0.088	0.070	0.018	-0.040, 0.076	
High [> 1749]	463	0.061	0.042	0.019	-0.038, 0.077	
HEI (0-100)						0.889
Low [<=52.7]	450	0.064	0.044	0.019	-0.040, 0.078	
High [>52.7]	473	0.083	0.069	0.025	-0.033, 0.082	

VAT, visceral adipose tissue volume (in liters); Kcal, kilocalories; HEI, Healthy Eating Index (range from 0-100).

Table S5. Effect of COVID-19 shutdown on follow-up MRIs.

Follow-up MRI scan	BEFORE shutdown	DURING shutdown	Total
Not done	38	34	72
Done	754	182	936
Within window	749	120	869
> 7 months	5	62	67
Total Participants	792	216	1008

From: The design and rationale of a multi-center randomized clinical trial comparing one avocado per day to usual diet: The Habitual Diet and Avocado Trial (HAT) [15].

Figure S1. Representative example of MRI image for VAT.

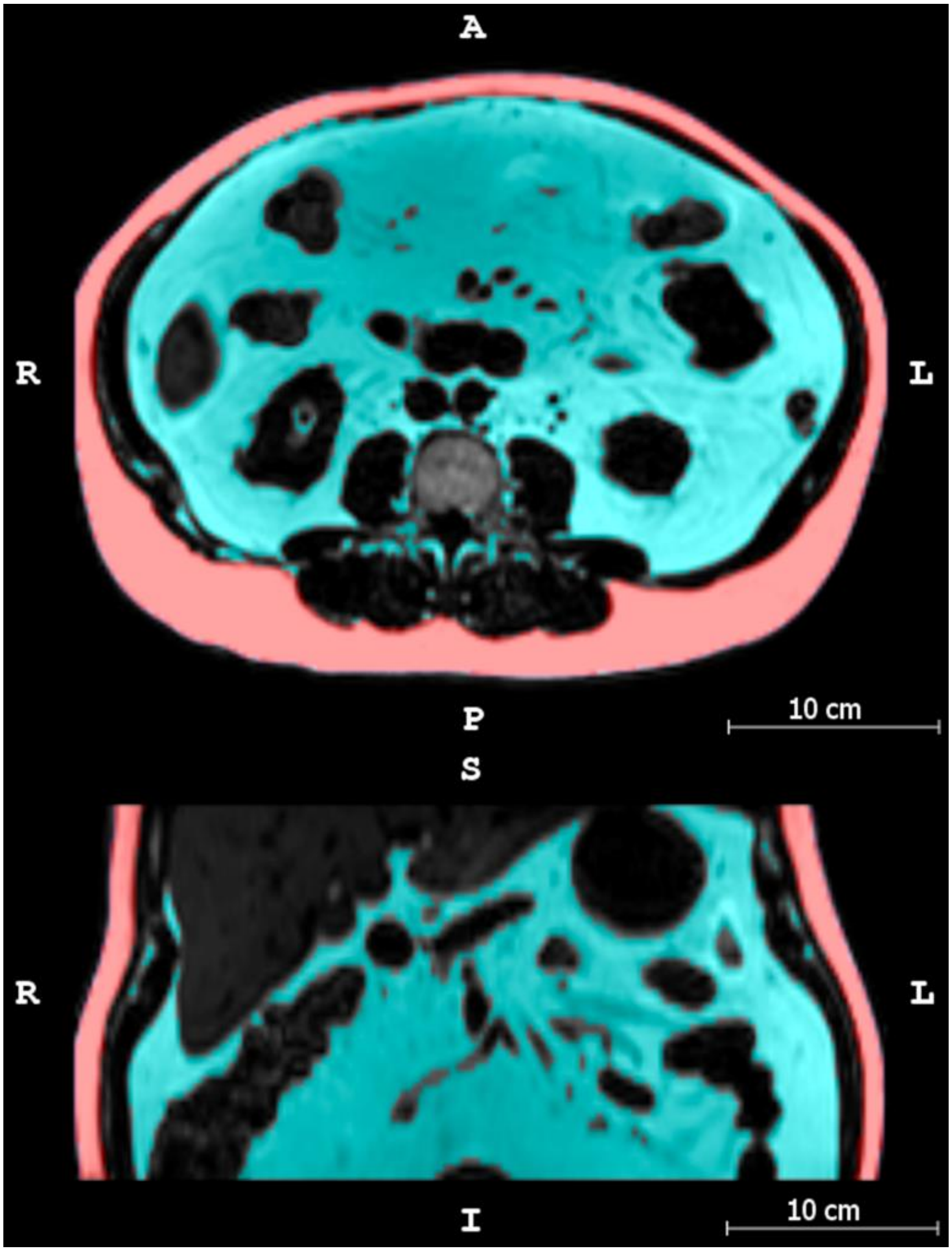
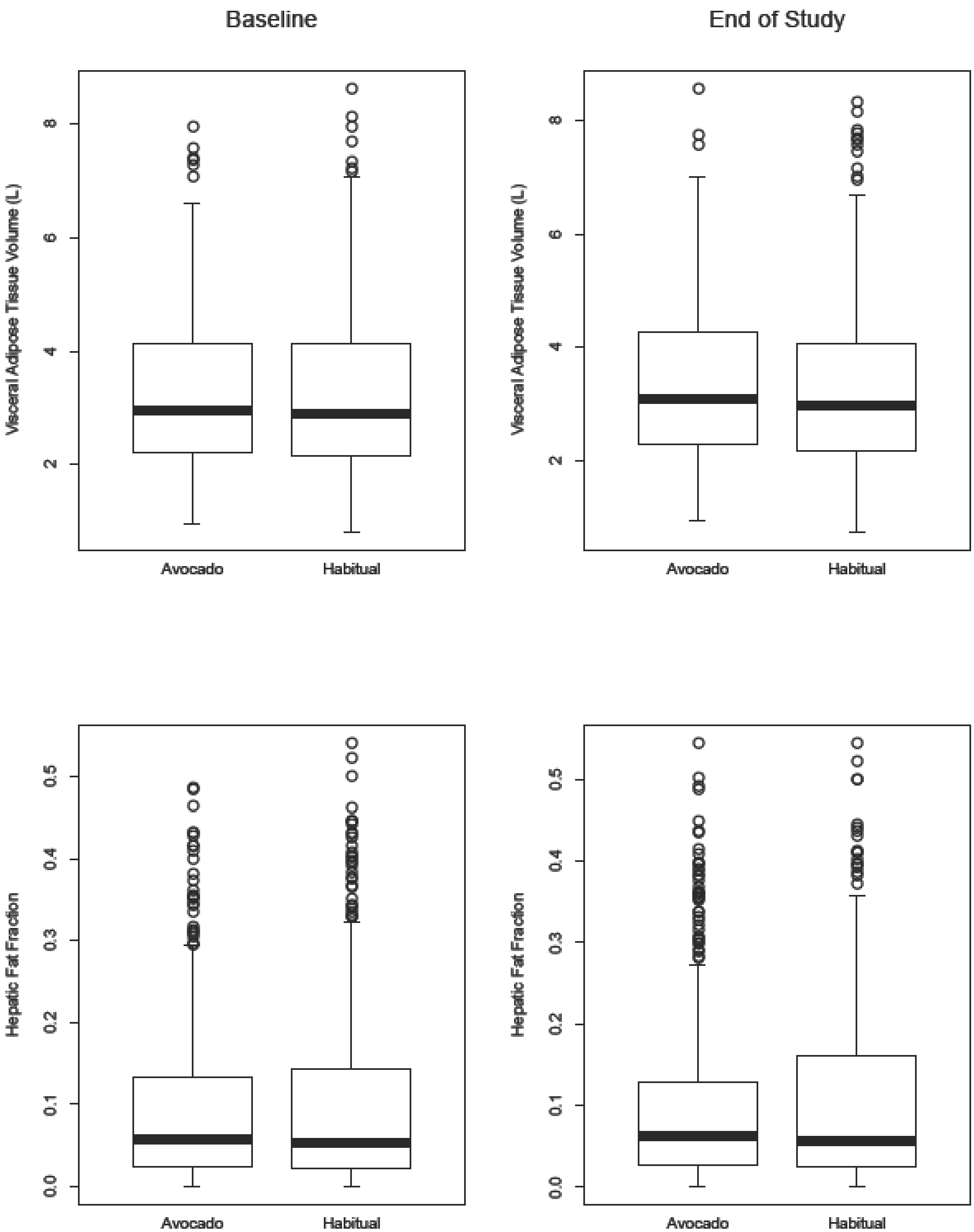


Figure S2. Boxplots for the VAT and HFF data at baseline and end of study, by arm.



Note: Data are presented as box plots. The box stretches from the 25th to the 75th percentile. The median is shown with a line across the box. The whiskers indicate 1.5 times the interquartile range above the third and below the first quartiles, or the upper or lower extreme values, whichever is closer. Open circles indicate observations outside the range of the upper whisker.